CDC HIV/AIDS Science Facts:

Male Circumcision and Risk for HIV Transmission: Implications for the United States

August 2006

This fact sheet summarizes information in 4 areas of male circumcision: (1) male circumcision and risk of HIV transmission; (2) male circumcision and other health conditions; (3) risks associated with male circumcision; and (4) status of HIV infection and male circumcision in the United States.

What is Male Circumcision?

Male circumcision is the surgical removal of some or all of the foreskin (or prepuce) from the penis [2].

Male Circumcision and Risk for HIV Transmission

Biologic Plausibility

Compared to the dry external skin surface, the inner mucosa of the foreskin has less keratinization (deposition of fibrous protein), a higher density of target cells for HIV infection (Langerhans cells) and is more susceptible to HIV infection in laboratory studies [3]. It has also been argued that the foreskin may have greater susceptibility to traumatic epithelial disruptions during intercourse, providing a portal of entry for pathogens, including HIV [4]. In addition, the microenvironment in the preputial sac between the unretracted foreskin and the glans penis may be conducive to viral survival [2]. Finally, the higher rates of sexually transmitted genital ulcerative

disease for uncircumcised men may also increase susceptibility to HIV infection [5].

International Observational Studies

Multiple cross-sectional, prospective, and ecologic (population-level) studies have identified lack of male circumcision as a risk factor for HIV infection.

A systematic review and meta-analysis focused on the heterosexual transmission of HIV in Africa was published in 2000 [6]. It included 19 cross-sectional studies, 5 case-control studies, 3 cohort studies, and 1 partner study. A substantial protective effect of male circumcision on risk for HIV infection was noted, along with a reduced risk for genital ulcer disease. After adjustment for confounding in the population-based studies, the relative risk for HIV infection was 44% lower in circumcised men. The strongest association was seen in high-risk men, such as sexually transmitted disease (STD) clinic patients, for whom the adjusted relative risk was 71% lower for circumcised men.

A review that included stringent assessment of 10 potential confounding factors and was stratified by study type or study population was published in 2004 [7]. Most of the studies were from Africa. Of the 35 observational studies included in the review, the 16 in the general population had inconsistent results. The 1 large prospective cohort study in this group showed a significant protective effect, with the odds of infection being 42% lower





in circumcised men [8]. The remaining nineteen studies were conducted in high-risk populations. These found a consistent, substantial protective effect, which increased with adjustment for confounding. Four of these were cohort studies: all demonstrated a protective effect; in 2 studies, the protective effect was statistically significant.

Ecologic studies also indicate a strong association between lack of male circumcision and HIV infection at the population level. Although links between circumcision, culture, religion, and risk behavior may account for some of the differences in HIV infection prevalence, countries in Africa and Asia where the prevalence of male circumcision is less than 20% have HIV infection prevalences several times higher than countries in those regions where more than 80% of men are circumcised [9].

International Clinical Trials

Three randomized, controlled clinical trials are being conducted (in 2006) or have recently been concluded in Africa to determine whether circumcision of adult males will reduce their risk for HIV infection. One of these 3 studies, conducted in South Africa, was stopped in 2005 after an interim analysis indicated a strong protective effect of circumcision [10]. Men who had been randomly assigned to the circumcision group had a 60% lower incidence of HIV infection compared with men who were assigned to a wait-list group to be circumcised at the end of the study. A few men who had been assigned to be circumcised did not undergo the procedure, and vice versa. When the data were reanalyzed to account for these deviations, the men who had been circumcised had a 76% reduction in risk for HIV infection compared with those who were not circumcised. The 2 other studies—in Kenya [11] and Uganda [12]—completed enrollment in 2005 and are scheduled to be completed in 2007. The Uganda study investigators are also examining (1) safety and acceptability of male circumcision in HIV-infected men and men of unknown HIVinfection status, (2) safety and acceptability

of male circumcision in the men's female sex partners, and (3) effect of male circumcision on male-to-female transmission of HIV and other STDs.

Male Circumcision and Male-to-Female Transmission of HIV

In an earlier study of couples in Uganda in which the male partner was HIV infected and the female partner was initially HIV-seronegative, the infection rates of the female partners differed by the circumcision status and viral load of the male partners. If the male blood HIV viral load was <50,000 copies/mL, there was no HIV transmission if the man was circumcised, compared a rate of 9.6 per 100 person-years if the man was not circumcised [8]. If viral load was not controlled, there was a statistically insignificant trend toward a reduction in the male-to-female transmission rate for circumcised men compared with uncircumcised men. The reduction may be due to decreased viral shedding from circumcised men or to a reduction in ulcerative sexually transmitted infections acquired by the female partners of circumcised men [13].

Male Circumcision and Other Health Conditions

Lack of male circumcision has also been associated with sexually transmitted genital ulcer disease, urinary tract infections in infants, penile cancer, and cervical cancer in female partners of uncircumcised men [2]. The 2 cancers are related to human papillomavirus (HPV) infection. Transmission of this virus is also associated with lack of male circumcision. A recent meta-analysis included 26 studies that assessed the association between male circumcision and risk for genital ulcer disease. Among circumcised men, the risk for syphilis and chancroid was significantly lower: the significance of the reduced risk for herpes simplex virus-2 infection was borderline [5].

Risks Associated with Male Circumcision

Reported complication rates depend on the type of study (e.g., chart review vs. prospective study), setting (medical vs. nonmedical facility), operator (traditional vs. medical practitioner), patient age (infant vs. adult), and surgical technique or instrument used. The most common complications are minor bleeding and local infection. In large studies of infant circumcision in the United States, complications rates range from 0.2 to 2.0% [2]. In the recently completed South African study of adult circumcision by general medical practitioners in their surgical offices, the overall complication rate was 3.8%. The most commonly reported complications were pain (0.8%), followed by swelling or hematoma, bleeding, and problems with appearance (each 0.6%). Damage to the penis (0.3%), infection (0.2%), and delayed wound healing (0.1%) were uncommon. There were no reported deaths or problems with urination [10].

HIV Infection and Male Circumcision in the United States

In 2004, men who have sex with men (MSM) (47%) and persons exposed through heterosexual contact (33%) accounted for an estimated 80% of all HIV/AIDS cases diagnosed in areas in the United States with confidential name-based HIV infection reporting. Blacks accounted for 49% of cases and Hispanics for 18%. Infection rates for both groups were several-fold higher than that for whites. An overall prevalence of less than 0.5% was estimated for the general population [14]. Although data on HIV infection rates since the beginning of the epidemic are available, data on circumcision and risk for HIV infection in the United States are limited. In 1 cross-sectional survey of MSM, lack of circumcision was associated with 2-fold increased odds of prevalent HIV infection [15]. In a prospective study of MSM, lack of circumcision was associated with

a 2-fold increased risk for HIV seroconversion [16]. In both studies, the results were statistically significant, and other risk factors were controlled. In one prospective study of heterosexual men at an urban STD clinic, when other risk factors were controlled, uncircumcised men had a 3.5-fold higher risk for HIV infection than did men who were circumcised. However, this association was not statistically significant [17].

Status of Male Circumcision in the United States

In a national probability sample of adults in 1992, the National Health and Social Life Survey found that 77% of men reported being circumcised, including 81% of white men, 65% of black men, and 54% of Hispanic men [18]. It is important to note that reported circumcision status may be subject to misclassification. In a study of adolescents, only 69% of circumcised and 65% of uncircumcised young men correctly identified their circumcision status as verified by physical exam [19].

According to the National Hospital Discharge Survey, 65% of newborns were circumcised in 1999, and the overall proportion of newborns circumcised was stable from 1979 to 1999 [20]. Notably, the proportion of black newborns circumcised increased during this period (58% to 64%); while the proportion of white infants circumcised remained stable (66%). In addition, the proportion of newborns who were circumcised in the Midwest increased during the 20-year period from 74% in 1979 to 81% in 1999; the proportion of infants born in the West who were circumcised decreased from 64% in 1979 to 37% in 1999. In another survey, the National Inpatient Sample, circumcision rates increased from 48% during 1988-1991 to 61% during 1997-2000. Circumcision was more common among newborns born to families of higher socioeconomic status. newborns in the Northeast or Midwest, and newborns who were black [21].

In 1999, the American Academy of Pediatrics (AAP) changed from routinely recommending circumcision to a neutral stance on circumcision. noting, "It is legitimate for the parents to take into account cultural, religious, and ethnic traditions, in addition to medical factors, when making this choice" [22]. This position was reaffirmed by the academy in 2005. This change in policy may influence reimbursement for, and practice of, neonatal circumcision. According to a 1995 review, 61% of circumcisions were paid by private insurance, 36% were paid for by Medicaid, and 3% were paid by the parents of the infant [23]. As of mid-2004, 48 of the 50 states' Medicaid programs reimbursed providers for circumcision, [24] although multiple states are considering eliminating Medicaid reimbursement for circumcision in light of the AAP statement and growing Medicaid budget constraints.

Considerations for the United States

A number of important differences must be considered in the possible role of male circumcision in HIV prevention in the United States. Notably, the overall risk for HIV infection is considerably lower in the United States. changing risk-benefit and cost-effectiveness considerations. Also, studies have focused on heterosexual, penile-vaginal sex, the predominant mode of HIV transmission in Africa, while the predominant mode of sexual HIV transmission in the United States is penile-anal sex among MSM. In addition, although the prevalence of circumcision may be somewhat lower in racial and ethnic groups with higher rates of HIV infection, most Americans are already circumcised, and it is not known whether men at higher risk for HIV infection would be willing to be circumcised or whether parents would be willing to have their infants circumcised to reduce possible future HIV infection risk. Lastly, whether the effect of male circumcision differs by HIV-1 subtype (predominately subtype B in the United States and subtypes A, C, and D in Africa) is also unknown.

Summary

In international observational studies and 1 randomized controlled trial, male circumcision was associated with lower risk for HIV infection. The results of 2 more clinical trials are expected in 2006 or 2007. To a lesser extent, male circumcision could also reduce male-to-female transmission of HIV. Circumcision has also been associated with a number of other health benefits. Although there are risks to male circumcision. serious complications are rare. Accordingly, male circumcision may play an important role in HIV prevention in settings similar to those of the clinical trials (i.e., in sub-Saharan Africa), depending on factors such as general willingness to be circumcised, cost-benefit calculations, and the potential effect of sexual risk taking by those who may overestimate the possible protective effect of circumcision.

At this time, CDC has no recommendation on male circumcision as a public health intervention for the prevention of HIV transmission in the United States and is undertaking additional consultation and research to evaluate the potential value, risks, and feasibility of circumcision as an HIV prevention intervention in the United States.

References

- 1. Fink AJ. A possible explanation for heterosexual male infection with AIDS. *N Engl J Med* 1986;315:1167.
- 2. Alanis MC, Lucidi RS. Neonatal circumcision: a review of the world's oldest and most controversial operation. *Obstet Gynecol Surv* 2004;59:379-395.
- 3. Patterson BK, Landay A, Siegel JN, et al. Susceptibility to human immunodeficiency virus-1 infection of human foreskin and cervical tissue grown in explant culture. *Am J Pathol* 2002;161:867-873.

- 4. Szabo R, Short RV. How does male circumcision protect against HIV infection? *BMJ* 2000;320(7249):1592-1594.
- 5. Weiss HA, Thomas SL, Munabi SK, Hayes RJ. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. *Sex Transm Infect* 2006;82:101-109; discussion 10.
- 6. Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. *AIDS* 2000 20;14:2361-2370.
- 7. Siegfried N, Muller M, Volmink J, et al. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2003(3): CD003362.
- 8. Gray RH, Kiwanuka N, Quinn TC, et al. Male circumcision and HIV acquisition and transmission: cohort studies in Rakai, Uganda. *AIDS* 2000;14:2371-2381.
- 9. Halperin DT, Bailey RC. Male circumcision and HIV infection: 10 years and counting. *Lancet* 1999;354:1813-1815.
- 10. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 trial. *PLoS Med*. 2005;2:e298.
- U.S. National Institutes of Health. Male circumcision and HIV rates in Kenya. 2006.
 Available from: http://www.clinicaltrials.gov/ct/show/NCT00059371. Accessed: March 27, 2006.
- 12. U.S. National Institutes of Health. Trial of Male Circumcision: HIV, Sexually Transmitted Disease (STD) and Behavioral Effects in Men, Women and the Community. 2006. Available from: http://www.clinicaltrials.gov/ct/show/NCT00124878?order=1. Accessed March 27, 2006.

- 13. Gray R, Wawer MJ, Thoma M, et al. Male circumcision and the risks of female HIV and sexually transmitted infections acquisition in Rakai, Uganda. 13th Conference on Retroviruses and Opportunistic Infections; 2006; Denver, CO. Available at: http://www.retroconference.org/2006/Abstracts/25977. htm.
- 14. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2004. Vol. 16. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2005. Available at: http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2004report.
- 15. Kreiss JK, Hopkins SG. The association between circumcision status and human immunodeficiency virus infection among homosexual men. *J Infect Dis* 1993;168:1404-1408.
- 16. Buchbinder SP, Vittinghoff E, et al. Sexual risk, nitrite inhalant use, and lack of circumcision associated with HIV seroconversion in men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2005;39:82-89.
- 17. Telzak EE, Chiasson MA, Bevier PJ, Stoneburner RL, Castro KG, Jaffe HW. HIV-1 seroconversion in patients with and without genital ulcer disease: a prospective study. *Ann Intern Med* 1993;119:1181-1186.
- 18. Laumann EO, Masi CM, Zuckerman EW. Circumcision in the United States. prevalence, prophylactic effects, and sexual practice. *JAMA* 1997;277:1052-1057.
- 19. Risser JM, Risser WL, Eissa MA, Cromwell PF, Barratt MS, Bortot A. Self-assessment of circumcision status by adolescents. *Am J Epidemiol* 2004;159:1095-1097.
- 20. Centers for Disease Control and Prevention. Trends in circumcision among newborns [fact sheet]. 2006; Available at: http://www.cdc.gov/nchs/products/pubs/pubd/hestats/circumcisions/circumcisions.htm. Accessed: March 27 2006.

- 21. Nelson CP, Dunn R, Wan J, Wei JT. The increasing incidence of newborn circumcision: data from the nationwide inpatient sample. *J Urol* 2005;173:978-981.
- 22. American Academy of Pediatrics, Task Force on Circumcision. Circumcision policy statement. *Pediatrics* 1999;103:686-693.
- 23. Mansfield CJ, Hueston WJ, Rudy M. Neonatal circumcision: associated factors and length of hospital stay. *J Fam Pract* 1995;41:370-376.
- 24. American Academy of Pediatrics. Medicaid reimbursement for commonly used pediatric services, 2004/05 interim report. 2004; Available from: http://www.aap. org/research/medreimPDF0405/Medicaid_Reimbursement_2004-05_Interim_Report. pdf. Accessed March 27, 2006.